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SEARCH REQUEST FORM

Scientific and Technical Information Center

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Art Unit: 1627 Phone Number 30 8-0732 Serial Number: 09/601,073
Mail Box and Bldg/Room Location: 3B01 7A11 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

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Searcher: JHW	NA Sequence (#)	STN ✓
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Date Searcher Picked Up: 5/13/02	Bibliographic ✓	Dr.Link
Date Completed: 5/13/02	Litigation	Lexis/Nexis
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PTO-1590 (8-01)

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FILE COVERS 1907 - 13 May 2002 VOL 136 ISS 20
FILE LAST UPDATED: 10 May 2002 (20020510/ED)

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L95 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:53732 HCAPLUS
DN 132:106966
TI Lupus **anticoagulant** antibody to F1 region of **prothrombin**
IN **Exner, Thomas**; Kraus, Michael
PA **Gradipore Limited, Australia**; Dade Behring Marburg G.m.b.H.
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K016-34
ICS C07K016-36; G01N033-86
CC 15-3 (Immunochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000002925	A1	20000120	WO 1999-AU556	19990709
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9947623	A1	20000201	AU 1999-47623	19990709
	AU 737928	B2	20010906		
	EP 1097174	A1	20010509	EP 1999-930930	19990709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	AU 1998-4603	A	19980710		
	WO 1999-AU556	W	19990709		

AB Isolated antibodies directed against the F1 region of **prothrombin**, which antibodies mimic the effect of a lupus **anticoagulant** (LA) in vitro , and uses of the antibodies in **blood clotting** tests.

ST mouse monoclonal antibody human **prothrombin** peptide; **blood clotting** test lupus **anticoagulant** antibody

IT **Venoms**
(Taipan; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT Bioassay
(Textarin test; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT Kaolin, biological studies
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(**blood clotting** time test; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT **Vipera russelli**
(dil. **Russell's viper venom** time test; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT Mouse
Protein sequences
(lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT Antibodies
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lupus **anticoagulants**; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT Antibodies
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT **Blood coagulation**
(test; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT 72162-96-0, **Thromboplastin**
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(**activated** partial **thromboplastin** time test; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT 9035-58-9, Tissue **thromboplastin**

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(inhibition test; lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT 9001-26-7, **Prothrombin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT 137053-43-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(lupus **anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Casipit, C; Protein Science 1998, V7, P1671 HCAPLUS
(2) Exner, T; Thrombosis and Haemostasis 1999, V81(3), P470 HCAPLUS
(3) Fleck, R; Blood 1988, V72(2), P512 MEDLINE
(4) Hursting, M; Clinical Chemistry 1993, V39(4), P583 HCAPLUS
(5) Pelzer, H; Thrombosis and Haemostasis 1991, V65(2), P153 HCAPLUS

L95 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:621222 HCAPLUS
DN 132:177284
TI Detecting APC-resistant **factor V**: a functional method without **plasma** dilution
AU Rylatt, D. B.; Hohnen-Behrens, C.; Pilgrim, R. L.; Dickeson, L. E.; Neal, M.; **Exner, T.**
CS **Gradipore Research Laboratories, North Ryde, Australia**
SO Blood Coagulation & Fibrinolysis (1999), 10(6), 359-366
CODEN: BLFIE7; ISSN: 0957-5235
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 9, 13, 14

AB A method for detecting **activated protein C** (APC)-resistant **factor V**, esp. **factor V Leiden**, is described, which uses reagents contg. two unfractionated **snake venoms**. The procedure can be used for testing **plasma** samples from patients receiving oral **anticoagulant** therapy, **heparin** therapy and patients with lupus **anticoagulant**, and does not require the use of **factor-V**-deficient **plasma**. The sample **plasma** is first **incubated** with dil. **venom** from **Agkistrodon contortrix contortrix** (Southern **Copperhead**) which **activates** the endogenous **protein C** and then a dil. **Russell's viper venom** time test is performed. In individuals with APC-resistant **factor V**, esp. **factor V Leiden**, a marginal prolongation of dil. **Russell's viper venom** time was noted [1.14.+-.0.14 s (n = 16)]. Non-carriers were easily discriminated in each patient group, with a prolongation of 2.69.+-.0.30 s for normal **blood** donors (n = 127), 2.61.+-.0.38 s for patients taking oral **anticoagulants** (n = 102), 2.41.+-.0.45 s for patients taking **heparin** (n = 96), and 2.38.+-.0.41 s for patients with lupus **anticoagulant** (n = 22). Patients taking oral **anticoagulants** with moderate prolongation (between 1.5- and 2.0-fold) may have low levels of functional **protein C**

and this might addnl. indicate a subgroup of such patients at higher than normal **thrombotic** risk.

ST **blood coagulation factor V**
Leiden assay **venom**

IT **Agkistrodon contortrix contortrix**
Anticoagulants
Vipera russelli
(detecting **activated protein C**-resistant **factor V** - a functional method without **plasma** diln.)

IT Antibodies
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(lupus **anticoagulants**; detecting **activated protein C**-resistant **factor V** - a functional method without **plasma** diln.)

IT **Venoms**
(**snake**; detecting **activated protein C**-resistant **factor V** - a functional method without **plasma** diln.)

IT **9001-24-5, Blood-coagulation factor V 166799-93-5, Blood-coagulation factor V Leiden**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(detecting **activated protein C**-resistant **factor V** - a functional method without **plasma** diln.)

IT 81-81-2, Warfarin **9005-49-6, Heparin**, biological studies
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(detecting **activated protein C**-resistant **factor V** - a functional method without **plasma** diln.)

IT **42617-41-4, Blood-coagulation factor XIVa**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(detecting **activated protein C**-resistant **factor V** - a functional method without **plasma** diln.)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

(1) Aboud, M; Br J Haematol 1997, V97, P798 MEDLINE
(2) Bertina, R; Nature 1994, V343, P1534
(3) Brandt, J; Thromb Haemost 1995, V74, P1185 HCAPLUS
(4) Chan, W; Blood 1998, V91, P1135 HCAPLUS
(5) Dahlback, B; Proc Natl Acad Sci USA 1993, V90, P1004 HCAPLUS
(6) De Ronde, H; Thromb Haemost 1994, V72, P880 HCAPLUS
(7) Gable, P; Thromb Res 1997, V86, P79 HCAPLUS
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(9) Jorquera, J; Lancet 1994, V344, P1162 MEDLINE
(10) Kalafatis, M; J Biol Chem 1994, V269, P31869 HCAPLUS
(11) Kraus, M; Thromb Res 1995, V79, P217 HCAPLUS
(12) Lewandowski, K; Thromb Res 1997, V85, P105 HCAPLUS
(13) Reitsma, P; Blood Coag Fibrinol 1996, V7, P659 HCAPLUS
(14) Ridker, P; N Engl J Med 1995, V332, P912 HCAPLUS

(15) Robert, A; Thromb Haemost 1996, V75, P562 HCAPLUS
(16) Shen, L; J Biol Chem 1994, V269, P18735 HCAPLUS
(17) Svensson, P; Thromb Haemost 1997, V77, P332 HCAPLUS
(18) Tripodi, A; Thromb Haemost 1997, V77, P436 HCAPLUS
(19) Van Oerle, R; Am J Clin Path 1997, V107, P521 HCAPLUS
(20) Van der Meer, F; Thromb Haemost 1997, V78, P631 HCAPLUS
(21) Williamson, D; Blood 1998, V91, P1140 HCAPLUS
(22) Zoller, B; J Clin Invest 1994, V94, P2521 MEDLINE

L95 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:495483 HCAPLUS
DN 131:127393
TI Improved **blood coagulation** test using whole dilute **Agkistrodon contortrix venom**
IN **Exner, Thomas**
PA **Gradipore Limited, Australia**
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-86
ICS C12Q001-56
CC **9-15 (Biochemical Methods)**
Section cross-reference(s): 7, 12
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9939212	A1	19990805	WO 1999-AU69	19990201 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2318250	AA	19990805	CA 1999-2318250	19990201 <--
AU 9924041	A1	19990816	AU 1999-24041	19990201 <--
EP 1068536	A1	20010117	EP 1999-903537	19990201 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002502040	T2	20020122	JP 2000-529615	19990201 <--
PRAI AU 1998-1596	A	19980202 <--		
WO 1999-AU69	W	19990201 <--		

AB A method of detg. the **coagulation** potential of a **plasma** sample comprising the steps of: (a) **preincubating** the **plasma** sample with whole dil. **Agkistrodon contortrix venom** (ACCV) or like reagent such that (i) endogenous **protein C** in the **plasma** is converted into **activated protein C** by the reagent, and (ii) adding **factor Xa** which is progressively inactivated by **antithrombin III/ heparin cofactor** (2) during the **preincubation**; (b) then adding reagents to initiate **clotting** comprising: (i) an exogenous reagent which **activates factor X** to **Xa** or **prothrombin** to **thrombin** in a **factor V** -dependent manner, and (ii) components, such as phospholipid and **calcium ions**, for efficient **coagulation**; (c) monitoring a reaction indicative of the rate of **coagulation**; (d) comparing the rate of **coagulation** detected in step (b) with the equiv. rate detd. for a normal patient, or comparing the rate of

coagulation detected in step (b) with the equiv. rate detd. for the **plasma** sample in the absence of **protein C activator**; and (e) detg. the **coagulation** potential of the **plasma** sample from one or other of the comparisons of step (d). The use of levels of 0.002-0.004% ACCV in the test allows the differentiation between **sera** from normal individuals from patients with impaired **clotting** function. Protac from Pentpharm AB did not work very well in the assay.

ST **blood coagulation** assay **Agkistrodon venom**

IT Phospholipids, biological studies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**clotting** reagent contg.; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **Blood analysis**
Blood coagulation
Blood plasma
Colorimetry
Fluorometry
Surfactants
(improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT Glycosaminoglycans, analysis
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in **preincubation** reagent; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT Antibodies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(lupus **anticoagulants**, nonspecific inhibitor, phospholipids to overcome; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT Detergents
(nonionic; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **Venoms**
(**snake**, in **preincubation** reagent; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT Buffers
Preservatives
(to reverse effect of **heparin**; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **Notechis**
Notechis scutatus
Oxyuranus scutellatus
Pseudonaja
Pseudonaja textilis
Vipera russelli
(**venom**, in **clotting** reagent; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **Agkistrodon bilineatus**
Agkistrodon contortrix
Agkistrodon contortrix laticinctus
Agkistrodon contortrix mokasen
Agkistrodon piscivorus
(**venom**, in **preincubation** reagent; improved **blood coagulation** test using whole dil.

Agkistrodon contortrix venom)

IT **60202-16-6, Protein C**
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**activation** of endogenous, reagent for; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **9001-26-7, Prothrombin 9001-29-0, Factor X**
RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**activation** of, reagent for; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **14127-61-8, Calcium ion**, biological studies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**clotting** reagent contg.; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **9001-24-5, Blood-coagulation factor V**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(differentiation of **factor V Leiden** and; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **166799-93-5, Blood-coagulation factor V Leiden**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(differentiation of normal **factor V** and; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **9000-94-6, Antithrombin III**
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**heparin cofactor 2** and, **factor Xa** in **preincubation** reagent inactivation by; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **9002-04-4, Thrombin**
RL: ARU (Analytical role, unclassified); FMU (Formation, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT 103469-93-8, Protac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **9002-05-5, Factor Xa**
RL: ARG (Analytical reagent use); FMU (Formation, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(in **preincubation** reagent; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT **9005-49-6, Heparin**, analysis **9042-14-2, Dextran sulfate 75634-40-1, Dermatan**

RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in **preincubation** reagent; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

IT 28728-55-4, Polybrene
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to reverse effect of **heparin**; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix venom**)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(2) Gradipore Ltd; AU 3105985 A 1996
(3) Kabivitrum; WO 9101382 A 1991 HCAPLUS
(4) Max Plank Ges Wissensch; DE 3724443 A 1989 HCAPLUS
(5) Ruzicka, K; Thrombosis Research 1997, V87(6), P501 HCAPLUS
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L95 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:730745 HCAPLUS
DN 130:136228
TI Methods for subtyping lupus **anticoagulants**
AU **Exner, T.**
CS **Gradipore Ltd., Sydney, 2113, Australia**
SO Lupus (1998), 7(Suppl. 2), S103-S106
CODEN: LUPUES; ISSN: 0961-2033
PB Stockton Press
DT Journal
LA English
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 14
AB Two simple procedures were tested for their potential to identify .beta.2-glycoprotein 1 (.beta.2GP1) or **prothrombin** cofactor dependence among lupus **anticoagulants** (LA). The first comprised mixing test **plasma** 1:4 with .beta.2GP1-deficient **plasma** instead of with normal **plasma**. .beta.2GP1 deficiency decreased, but did not abolish most LA detectable in KCT, DRVVT and APTT **clotting** tests. Mixing 1:4 with bovine **plasma** was evaluated in a second test based on the KCT in the expectation that **prothrombin**-dependent LA would be preferentially shortened. Bovine **plasma** had a similar correcting effect on LA in all three tests considered here. Conversely, a **prothrombin** antibody was found to have similar prolonging effect on all three of these tests. LA patient **plasmas** displayed considerable heterogeneity when analyzed using a combination of these two tests. The clin. significance of these tests remains uncertain. DRVVT and KCT tests do not appear to discriminate .beta.2GP1-dependent from **prothrombin**-dependent LA.
ST lupus **anticoagulant** subtyping **blood coagulation** time APTT DRVVT KCT

IT **Blood coagulation**
(**Activated** Partial **Thromboplastin** Time (APTT), Dil. **Russell Viper Venom** Time (DRVVT), Kaolin **Clotting** Time (KCT); **blood coagulation** methods for subtyping lupus **anticoagulants**)

IT Apolipoproteins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(H, .beta.2-glycoprotein 1 dependent lupus **anticoagulant**; **blood coagulation** methods for subtyping lupus **anticoagulants**)

IT **Blood** analysis
(**blood coagulation** methods for subtyping lupus **anticoagulants**)
IT Antibodies
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lupus **anticoagulants**; **blood coagulation** methods for subtyping lupus **anticoagulants**)
IT 9001-26-7, **Prothrombin**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(dependent lupus **anticoagulant**; **blood coagulation** methods for subtyping lupus **anticoagulants**)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Arnout, J; Thromb Haemost 1998, V79, P79 HCAPLUS
(2) Brandt, J; Thromb Haemost 1995, V74, P1185 HCAPLUS
(3) Derksen, R; Ann Rheum Dis 1988, V47, P364 MEDLINE
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L95 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:722802 HCAPLUS
DN 130:195343
TI **Determination** of lupus **anticoagulant** (LA)
AU Yasumuro, Yoko
CS Department of Clinical Testings, Saint Marianna Medical University, Japan
SO Medical Technology (Tokyo) (**1998**), 26(10), 1133-1139
CODEN: METCDS; ISSN: 0389-1887
PB Ishiyaku Shuppan
DT Journal; General Review
LA Japanese
CC 15-0 (Immunochemistry)
AB A review with 9 refs. A review with 9 refs. describing the present state of the lupus **anticoagulant** (LA) or antiphospholipid antibody (aPL) tests. APL antigens comprise **prothrombin**, .beta.2-glycoprotein 1 (.beta.2GP1), **protein C**, protein S, and annexin **V**. LA acts as an **anticoagulant** in vitro, but produces **clotting** in vivo. The tissue **thromboplastin** inhibition test (TTI), dild. **activated** partial **thromboplastin** time (dAPTT), kaolin **clotting** time (KCT), dild. **Russell's viper venom** time (DRVVT), platelet neutralization procedure (PNP), and hexagonal (II) phosphatidyl ethanolamine tests for LA are described. The author suggests that low d. phospholipid tests such as TTI or dAPTT should be used for screening, and neutralization tests such as the PNP test, for confirmation. LA testing plays an important role for diagnosis of both **coagulant** diseases (e.g. SLE), and **noncoagulant** diseases, such as cardiac arrest or **thrombosis**.
ST review lupus **anticoagulant** test diagnosis disease
IT Heart, disease
(arrest; lupus **anticoagulant** (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)
IT Diagnosis

Thrombosis
(lupus **anticoagulant** (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)

IT Antibodies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(lupus **anticoagulants**; lupus **anticoagulant** (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)

IT Lupus erythematosus
(systemic; lupus **anticoagulant** (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)

L95 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:678826 HCAPLUS
DN 130:62727
TI A modified functional **global test** to measure **protein C**, protein S **activities** and the **activated protein C**-resistance phenotype
AU Gemmati, Donato; Serino, Maria L.; Scapoli, Gian L.
CS Centre for the Study of Haemostasis and Thrombosis, University of Ferrara, Ferrara, I-44100, Italy
SO Thrombosis Research (**1998**), 92(3), 141-148
CODEN: THBRAA; ISSN: 0049-3848
PB Elsevier Science Inc.
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 14
AB Identifying a defect affecting the **protein C**/protein S (PC/PS) **anticoagulant** system, using a single global test, has recently become possible thanks to a new methodol. approach based on the **activation** of endogenous **plasma** PC by Protac, derived from **Agkistrodon** Contortix **snake venom** (ACV). The introduction of a com. test (ProC Global), ACV-based, provides a useful tool for the screening of **thrombotic** patients since the most frequent causes of inherited **thrombophilia** are found in the PC/PS system. The test provides information only on the global **activity** of the **anticoagulant** pathway but not on PC and PS **activity** or on the **factor V** related conditions (e.g., FV **Leiden**). The present study shows that by carrying out the test alternating the presence of PC-, PS-, or FV-deficient **plasma** and using appropriate amts. of ACV, it is possible to increase the specificity of the test to correctly evaluate resp. the PC or PS **activities** or the **activated protein C** resistance condition (APC-R). These simple modifications applied to the original com. test allow to detect exactly, using a single, basic methodol., the principal defects affecting the PC/PS **anticoagulant** pathway. Furthermore, carrying out the tests on an automated **coagulometer**, in combination or not with the classic ProC Global assay, it is possible to use a unique reagent profile to simultaneously investigate in the same or different samples, the PC, PS, and APC-R defect.
ST functional global test **protein C** S; **activity** resistance phenotype
IT **Blood-coagulation factors**
RL: ANT (Analyte); ANST (Analytical study)
(protein S; a modified functional global test to measure **protein C**, protein S **activities** and **activated protein C**-resistance phenotype)
IT **9001-24-5, Blood-coagulation factor V 42617-41-4, Blood coagulation factor XIVa**

RL: ANT (Analyte); ANST (Analytical study)
(a modified functional global test to measure **protein** C, protein S **activities** and **activated protein** C-resistance phenotype)
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(7) Francis, R; Thromb Res 1983, V32, P605 HCAPLUS
(8) Gemmati, D; Blood Coag Fibrinolysis 1997, V8, P118 MEDLINE
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(17) Preda, L; Blood Coag Fibrinolysis 1996, V7, P465 HCAPLUS
(18) Preda, L; S Thromb Res 1990, V60, P19 HCAPLUS
(19) Robert, A; Thromb Haemost 1996, V75, P562 HCAPLUS
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(22) Varadi, K; Br J Haematol 1995, V90, P884 HCAPLUS
(23) Wiesel, M; Thromb Res 1990, V58, P461 MEDLINE
(24) Wolf, M; Thromb Haemost 1989, V62, P1144 HCAPLUS

L95 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:557080 HCAPLUS
DN **129:299703**
TI Use of **snake venom** fractions in the **coagulation** laboratory
AU Marsh, N. A.
CS Research Concentration in Biomedical Science School of Life Sciences, Queensland University of Technology, Brisbane, QLD 4001, Australia
SO Blood Coagulation Fibrinolysis (**1998**), 9(5), 395-404
CODEN: BLFIE7; ISSN: 0957-5235
PB Lippincott-Raven Publishers
DT Journal; General Review
LA English
CC **9-0 (Biochemical Methods)**
AB A review with 119 refs. **Snake venom** toxins are now regularly used in the **coagulation** lab. for assaying hemostatic parameters and as **coagulation** reagents. **Snake venom thrombin**-like enzymes (SVTLE) are used for fibrinogen and fibrinogen breakdown product assay as well as detecting dysfibrinogenemias. Significantly, because SVTLE are not inhibited by **heparin**, they can be used for defibrinating samples that contain the **anticoagulant** before assay of hemostatic variables. **Prothrombin activators** are found in many **snake venoms** and are used in **prothrombin** assays, for studying **dysprothrombinemias** and prepg. **meizothrombin** and non-enzymic **prothrombin**. **Russell's viper** (Daboia **russelli**) **venom** (RVV) contains a no. of compds. useful in the assay of **factors V**, VII, **X**, platelet **factor** 3 and lupus **anticoagulants**. **Activators** from the taipan, Australian brown **snake** and saw-scaled **viper** have been used to assay lupus **anticoagulants**. **Protein C** and

activated protein C resistance can be measured by means of RVV and Protac, a fast acting inhibitor from Southern **copperhead snake venom** and von Willebrand **factor** can be studied with Botrocetin from Bothrops jararaca **venom**. Finally, phospholipase A2 enzymes and the disintegrins, a family of Arg-Gly-Asp (RGD)-contg. proteins found in **snake venoms**, show great potential for the study of hemostasis including, notably, platelet glycoprotein receptors GPIIb/IIIa and Ib.

ST review **snake venom coagulation**

IT **Coagulation (blood)**
Snake venoms
(use of **snake venom** fractions in **coagulation** lab.)

L95 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:653125 HCAPLUS
DN **127:328522**
TI Evaluation of a new screening assay ProC Global for identification of defects in the **protein C**/protein S **anticoagulant** pathway
AU Ruzicka, Katharina; Kapiotis, Stylianos; Quehenberger, Peter; Handler, Sylvia; Pabinger-Fasching, Ingrid; Mannhalter, Christine; Jilma, Bernd; Speiser, Wolfgang
CS Clinical Institute of Medical and Chemical Laboratory Diagnostics, University of Vienna, Vienna, A-1090, Austria
SO Thromb. Res. (**1997**), 87(6), 501-510
CODEN: THBRAA; ISSN: 0049-3848
PB Elsevier
DT Journal
LA English
CC **9-2** (**Biochemical Methods**)
Section cross-reference(s): 14
AB In the present study a new assay, ProC Global, globally estg. the **activity** of the main **plasma** components of **anticoagulant protein C**/protein S pathway, was evaluated with respect to test characteristics and its sensitivity in the detection of deficiency states of **protein C** and protein S and of increased **activated protein C** resistance (aPCR). In the ProC Global assay procedure, **protein C** is **activated** in patient's **plasma** by an **activator** reagent (**venom** from **Agkistrodon contortrix**). The extent of the prolongation of a sample's aPTT, caused by the **activation** of **protein C**, is taken as a measure for its **anticoagulant** capacity. Some 98 patients with one of the above mentioned defects were investigated. Decreased **plasma protein C activity** and increased aPCR were detected with a sensitivity of 1.0, while only 11 of 14 patients with decreased levels of free protein S antigen showed abnormal results in the ProC Global assay (sensitivity = 0.79). The test can be used in heparinized samples up to 1.0 anti **Xa** U/mL **heparin** (UFH and LMWH). When samples from patients on oral **anticoagulant** treatment are predild. with **factor V**-deficient **plasma** the test is sensitive for increased aPCR.

ST **anticoagulant** screening assay ProC Global; **protein C** S **anticoagulant** defect screening; **thrombosis** ProC Global screening assay

IT Protein S (**blood coagulation factor**)
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(-**protein C** pathway; ProC Global screening assay for identifying defects in **protein C**/protein S **anticoagulant** pathway)

IT **Coagulation (blood)**
Thromboembolism
Thrombosis
(ProC Global screening assay for identifying defects in **protein** C/protein S **anticoagulant** pathway)
IT Lupus **anticoagulant**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ProC Global screening assay for identifying defects in **protein** C/protein S **anticoagulant** pathway)
IT **Anticoagulants**
(oral; ProC Global screening assay for identifying defects in **protein C**/protein S **anticoagulant** pathway)
IT **60202-16-6, Protein C**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(-protein S pathway; ProC Global screening assay for identifying defects in **protein C**/protein S **anticoagulant** pathway)
IT **42617-41-4, Activated protein C**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ProC Global screening assay for identifying defects in **protein** C/protein S **anticoagulant** pathway)

L95 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:132846 HCAPLUS
DN **126:141755**
TI **Thrombosis** risk test
IN Campbell, Paula A.; Preda, Luigi
PA Instrumentation Laboratory, S.P.A., Italy; Campbell, Paula A.; Preda, Luigi
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-86
ICS C12Q001-56
CC **9-2** (**Biochemical Methods**)
Section cross-reference(s): 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9642018	A1	19961227	WO 1996-US9036	19960606 <--
	W: CA, JP, MX, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5780255	A	19980714	US 1995-488510	19950609 <--
	CA 2224465	AA	19961227	CA 1996-2224465	19960606 <--
	EP 830608	A1	19980325	EP 1996-919107	19960606 <--
	EP 830608	B1	20001004		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
	JP 11504718	T2	19990427	JP 1996-503149	19960606 <--
	AT 196804	E	20001015	AT 1996-919107	19960606 <--
	ES 2152531	T3	20010201	ES 1996-919107	19960606 <--
	JP 3248621	B2	20020121	JP 1997-503149	19960606 <--
PRAI	US 1995-488510	A	19950609 <--		
	WO 1996-US9036	W	19960606 <--		

AB The method involves detg. the **activity** of **protein C** and protein S in the **plasma** of an individual thought to be at **thrombotic** risk by adding to a **plasma** sample obtained from the individual: (1) a first reagent in an amt. sufficient to induce or **activate coagulation** in the **plasma**, (2) a second reagent which **activates** endogenous

protein C in the **plasma**, and (3) a third reagent comprising **calcium** salts, phospholipids or tissue **thromboplastin**, or a combination thereof. To a second **plasma** sample from the same subject is added a reagent which induces or **activates coagulation**, and a buffer or other material which does not **activate protein C**, and a third reagent as described above. The time, rate or both necessary for the conversion of endogenous fibrinogen to fibrin in both the first and second samples is measured. The same steps are performed on normal control **plasma**, and the difference or ratio in the times, rates, or both obtained above are detd. The difference or ratio is indicative of the **thrombotic** risk in the subject. A kit adapted to carry out the method also is the subject of the present invention. The methods and kits of the invention in other embodiments may comprise a first reagent comprising a synthetic substrate, a second reagent which in the first sample from the subject **activates protein C**, and in the second sample, a second reagent which does not **activate protein C**. In these embodiments, the rates of hydrolysis of the synthetic substrates are measured and compared.

ST **thrombosis** risk test kit; **plasma protein C** detn **thrombosis** risk; protein S detn **plasma thrombosis** risk

IT **Blood analysis**
Coagulation (**blood**)
Thrombosis
Venoms
(**protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

IT Protein S (**blood coagulation factor**)
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

IT Phospholipids, biological studies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

IT Fibrins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

IT Fibrinogens
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

IT **Agkistrodon contortrix contortrix**
(**venom**; **protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

IT **60202-16-6**, **Protein C**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

IT 7440-70-2D, **Calcium**, salts **9002-05-5**, **Factor Xa** 9035-58-9, Tissue **thromboplastin** 37316-87-3, **Blood-coagulation Factor** IXa
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**protein C** and protein S detn. in **blood plasma** in **thrombosis** risk test)

L95 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:171960 HCAPLUS
DN **124:197727**
TI Process for the detection of disorders of the **protein C** /protein S system
IN Kraus, Michael
PA Behringwerke Aktiengesellschaft, Germany
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM C12Q001-56
CC **9-2 (Biochemical Methods)**
Section cross-reference(s): 13
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 696642	A1	19960214	EP 1995-111554	19950722	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, PT, SE					
	DE 4427785	A1	19960215	DE 1994-4427785	19940808	<--
	CA 2155503	AA	19960209	CA 1995-2155503	19950804	<--
	US 5726028	A	19980310	US 1995-511248	19950804	<--
	AU 9528416	A1	19960222	AU 1995-28416	19950807	<--
	AU 694931	B2	19980806			
	JP 08089293	A2	19960409	JP 1995-200783	19950807	<--
PRAI	DE 1994-4427785		19940808	<--		

AB A method for detection of disorders of the **protein C** /protein S system comprising qual. or quant. detn. of functioning of **protein C**/protein S of the **blood coagulation** system in a biol. fluid is described. A **protein C activator** is added to the biol. sample; a contact phase **activator** is optionally added; the reaction mixt. is **incubated**; the **coagulation** reaction is started by addn. of **Ca2+** and/or other **blood coagulation**-inducing agents; and the **coagulation activity** is detd. The **protein C activator** is preferably a **snake venom** enzyme, e.g. those from **Agkistrodon**. The **coagulation activity** is measured by detn. of **activated**, partial **thromboplastin** time, **thromboplastin** time, or **Russell's viper venom** time.
ST **blood coagulation** disorder **protein C** S; C S protein system defect assay
IT Kaolin, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(contact phase **activator**; process for detection of disorders of **protein C**/protein S system)
IT **Blood coagulation**
(process for detection of disorders of **protein C** /protein S system)
IT Glass, oxide
Phospholipids, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(process for detection of disorders of **protein C** /protein S system)
IT **Agkistrodon**
Agkistrodon contortrix contortrix
(**protein C activator** of **venom** of; process for detection of disorders of **protein C** /protein S system)
IT **Blood-coagulation factors**
RL: ANT (Analyte); ANST (Analytical study)

(protein S, process for detection of disorders of **protein C**/protein S system)

IT 476-66-4, Ellagic acid 7631-86-9, Silica, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(contact phase **activator**; process for detection of disorders of **protein C**/protein S system)

IT **60202-16-6, Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(process for detection of disorders of **protein C** /protein S system)

IT 7440-70-2, **Calcium**, analysis **9001-24-5, Blood -coagulation factor V 9001-29-0, Factor X** 9035-58-9, **Blood-coagulation factor** III
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(process for detection of disorders of **protein C** /protein S system)

L95 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:29360 HCAPLUS
DN 124:139313
TI A more discriminating test for APC resistance and a possible **screening** test to include **protein C** and protein S
AU Denson, K. W. E.; Haddon, M. E.; Reed, S. V.; Davidson, S.; Littlewood, T. J.
CS Thame Thrombosis Haemostasis Research Foundation, Thame, OX9 3NY, UK
SO Thromb. Res. (**1996**), 81(1), 151-6
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 14
AB The abnormal **activated Protein C** (APC) cofactor recognized by Dahlback and colleagues, as a cause of APC resistance, is now known to be due to a mutation in the **Factor V** mol. resulting in a defect in the APC cofactor, termed **Factor V Leiden**. By adding exogenous APC to an **Activated** Partial **Thromboplastin** Time (APTT) reagent, Dahlback introduced the ratio of APC.APTT/ordinary APTT as a diagnostic test. A ratio of >2.0 indicated normal APC cofactor and a ratio of <2.0 indicated an APC cofactor defect. Addn. of preformed APC to **plasma**, by-passes endogenous **Protein C** (PC) and Protein S (PS). To characterize the three different defects, PC, PS and APC cofactor, it is necessary to perform three sep. specific assays as part of a **thrombophilia** screen. PC in the presence of PS can be **activated** to APC by PC **activators** (PCA) either by **thrombin/thrombomodulin**, or by **venom** fractions from a variety of **snakes** including **Agkistrodon Contortrix**. When PCA is added to **plasma**, the **active** inhibitor which destroys **Factors** Va and VIIIa, is generated by endogenous PC, PS and APC cofactor and in the presence of normal levels of PC and PS, the addn. of PCA to **plasma** will detect abnormality in the APC cofactor. The advantage of using PCA in the test system is that it is easier to prep. and standardize, and is more stable than APC. The authors have investigated the possibility of using the addn. of PCA instead of APC to **plasma** as a screening test for the APC inhibitor pathway, and in the presence of normal levels of PC and PS, as a test for APC resistance.
ST APC resistance screening **protein C** S
IT Proteins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(a more discriminating test for APC resistance and a possible screening test to include **protein C** and protein S)

IT **42617-41-4, Blood coagulation factor XIVa**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a more discriminating test for APC resistance and a possible screening test to include **protein C** and protein S)

L95 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:780909 HCAPLUS
DN 123:164278
TI Diagnostic methodologies for circulating **anticoagulants**
AU **Exner, Thomas**
CS Haematology Department, Westmead Hospital, Westmead, Australia
SO Thromb. Haemostasis (1995), 74(1), 338-44
CODEN: THHADQ; ISSN: 0340-6245
DT Journal; General Review
LA English
CC 9-0 (Biochemical Methods)
Section cross-reference(s): 14, 15
AB A review with 59 refs. Various types of circulating **anticoagulant** are encountered in **coagulation** testing labs. Those assocd. with bleeding often cause problems in diagnosis. The most common type of acquired **coagulation** inhibitor not assocd. with bleeding is the so-called lupus **anticoagulant** (LA). Differing from systemic lupus erythematosus (SLE) which occurs predominantly in women, primary LA occurs both in females and males. LA are now frequently sought in patients with recurrent fetal losses and acquired **thrombotic** problems as a causative **factor**, whereas in the past they are recorded as a lab. nuisance. Due to the complicating effect of inhibitors on **clotting** tests, diagnosis of various **coagulation** inhibitors remains difficult. There may also be significant overlap between different types of inhibitors. With the recent interest shown in LA, almost all non-specific inhibitors tend to be classed as LA. LA are defined as phospholipid-interfering antibodies. Current criteria have recently been confirmed and include screening with phospholipid-response tests, abnormal mixing studies and correction with phospholipids. However it is becoming clear that even LA as defined may be heterogeneous. Most LA are not directed at neg.-charged phospholipids alone as originally suggested, but rather at complexes of either beta-2-glycoprotein I or **prothrombin** with such phospholipids. There may also be other lipid-assocd. antigens involved. Although earlier work suggests that all LA functioned through a similar mechanism, there is now some preliminary evidence suggesting that various subclasses of LA may account for discrepant results sometimes obtained with different **clotting** tests. A variety of improvements to the basic screening tests for LA (APTT, KCT, DTTI and DRVVT) have recently been suggested. Phospholipid correction or LA-confirmatory tests based on these for the more reliable diagnosis of LA, even in complex clin. conditions have recently become available. Two of the more specific tests for LA recently developed are based on the **factor X activator** from **Russell's viper venom** and **prothrombin activators** from Australian elapid **venoms**.
ST review lupus **anticoagulant** detn diagnosis
IT Antibodies
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lupus **anticoagulant**; diagnostic methodologies for circulating **anticoagulants** in humans)
IT **Anticoagulants** and **Antithrombotics**
(lupus-assocd.; diagnostic methodologies for circulating **anticoagulants** in humans)

L95 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:333761 HCAPLUS
DN 122:103382
TI Some recent developments with lupus **anticoagulants**
AU **Exner, T.**
CS Hemostasis Ref. Lab., Westmead hosp., Sydney, 2145, Australia
SO Blood Coagulation Fibrinolysis (1994), 5(2), 281-9
CODEN: BLFIE7; ISSN: 0957-5235
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
AB A review with 59 refs. Lupus **anticoagulants** (LA) have been defined as phospholipid-interfering antibodies. Testing for them has become a frequently requested procedure in **coagulation** labs. and new methods have recently become available. **Activated** partial **thromboplastin** time (aPTT) reagents with reduced levels or different types of phospholipid provide high sensitivity. Correction procedures resistant to **heparin** and based on aPTT and dil. **Russell's viper venom** time (DRVVT) tests with added hexagonal phase phospholipids have improved the specificity of testing. Simplified tests based on **venom activators** of **factor X** and **prothrombin** improve the reliability of LA testing and may facilitate the further categorization of circulating **anticoagulants**. Recent studies on the mechanism of LA derived from various patients have confirmed their heterogeneity, principally in the cofactors involved in their interactions with phospholipids. Perhaps one-third of LA require beta2-glycoprotein 1 to exert an **anticoagulant** effect. The remainder may require human **prothrombin** as suggested from studies with reconstituted **clotting factor** systems.
ST review lupus **anticoagulant** antibody
IT Antibodies
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); ANST (Analytical study); BIOL (Biological study)
(lupus **anticoagulants**, action and detn. and clin. aspects of)

L95 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:598160 HCAPLUS
DN **119:198160**
TI Evaluation of a new **coagulation** test for **protein C**
AU Kolde, Hans Juergen; Pabinger-Fasching, I.; Darnell, L.; Koder, S.; Simmoteit, R.
CS Baxter Dtschl. G.m.b.H., Unterschleissheim, W-8044, Germany
SO Klin. Labor (**1992**), 38(12), 665-70
CODEN: KLLAEA
DT Journal
LA German
CC 7-1 (Enzymes)
Section cross-reference(s): **9**
AB An automated **coagulation** test for the detn. of **protein C** (PC) **activity** in human **blood plasma** is described, which is based on the measurement of **activated** partial **thromboplastin** time (aPTT) prolongation following **activation** with a PC **activator** partially purified from **copperhead snake venom**. Human PC-deficient **plasma** (prepd. by immunoadsorption) was employed to dil. samples and calibrants. Linear calibration curves were obtained between aPPT prolongation and PC **activities** for various mech. or optical **coagulators**; within and between series precisions were 4.5 and 3.3%, resp. Furthermore, the assay discriminated between subjects with hereditary PC deficiency and normal subjects and compared well with other methods for **plasmas** from subjects with or without deficiency and

on oral **anticoagulant** treatment. **Heparin** at therapeutic levels did not influence the results.

ST **protein C** detn **blood coagulation** test

IT **Blood analysis**
(**protein C** detn. in, of human, **coagulation** test for)

IT **60202-16-6, Blood coagulation factor XIV**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in human **blood plasma**, **coagulation** test for)

L95 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:534380 HCAPLUS
DN 119:134380
TI **Methods and kits for determination of protein C** using **thrombomodulin-thrombin** complexes
IN Funayama, Masashi
PA Funayama Masashi, Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C12Q001-56
ICS C12Q001-37
CC 7-1 (Enzymes)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 05130900	A2	19930528	JP 1991-352560	19911111 <--

AB A method and a kit for detn. of **protein C** using the immobilized the **thrombomodulin-thrombin** complex are disclosed. The complex can be immobilized on carriers, e.g., test tubes, beads, filter papers, etc., for **activation** of **protein C** prior to assay with conventional methods. The method is more convenient and accurate than the prior arts using **snake venom**.

ST **thrombomodulin thrombin** complex **protein C** detn

IT Immobilization, biochemical
(of **thrombomodulin-thrombin** complex, for **protein C** detn.)

IT Glycoproteins, specific or class
RL: PROC (Process)
(**thrombomodulins**, complexes, with **thrombin**, immobilization of, for **protein C** detn.)

IT **60202-16-6, Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **thrombomodulin-thrombin** complexes for)

IT **9002-04-4D, Thrombin**, complexes with **thrombomodulins**
RL: PROC (Process)
(immobilization of, for **protein C** detn.)

IT 139691-92-2, Serine protease inhibitor
RL: ANST (Analytical study)
(**protein C** detn. kit contg. **thrombomodulin -thrombin** complex and)

L95 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1992:168685 HCAPLUS
DN 116:168685

TI A novel **functional assay** of **protein C** in human **plasma** and its **comparison** with amidolytic and **anticoagulant** assays
AU Guglielmone, H. A.; Vides, M. A.
CS Fac. Cienc. Quim., Univ. Nac. Cordoba, Cordoba, 5016, Argent.
SO Thromb. Haemostasis (**1992**), 67(1), 46-9
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 13
AB A simple and fast method for the quant. detn. of **protein C activity** in **plasma** is here described. The first step consists in the conversion of **protein C** in the test sample into **activated protein C** by means of an **activator** isolated from Southern **Copperhead venom**. Subsequently, the degrdn. of **factor** Va, in presence of **protein C**-deficient **plasma**, is measured by the prolongation of the **prothrombin** time which is proportional to the amt. of **protein C** in the sample. The dose-response curve showed a linear relationship from 6 to 150% **protein C activity** and the inter- and intra-assay reproducibility was 3.5% and 5.6% resp. In normal subjects, a mean of **protein C** level of 98% of normal pooled **plasma** was found. Comparison with the **anticoagulant** assay in samples of patients with oral **anticoagulant**, liver cirrhosis, disseminated intravascular **coagulation** and severe preeclampsia revealed an excellent correlation ($r = 0.94$, $p < 0.001$). Also, a similar correlation ($r = 0.93$, $p < 0.001$) existed between amidolytic assay and the method here proposed for all the samples studied without including the oral **anticoagulant** group. These results allow the inference that this method evaluates the ability of **protein C** to interact with protein S, phospholipids, **calcium ions** and **factor** Va.
ST **protein C** detn **blood** analysis human
IT **60202-16-6, Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in **blood** anal. of human)

L95 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:602734 HCAPLUS
DN **115:202734**
TI Method of determining levels of extrinsic and intrinsic **clotting factors** and **protein C**
IN Carroll, James J.; Autenrieth, Stephen M.
PA Ortho Diagnostic Systems, Inc., USA
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM G01N033-86
ICS C12Q001-56
CC **9-2 (Biochemical Methods)**
Section cross-reference(s): 7
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 434377	A1	19910626	EP 1990-313862	19901218	<--
	EP 434377	B1	19950823			
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE					
	US 5169786	A	19921208	US 1989-452802	19891219	<--
	CA 2032561	AA	19910620	CA 1990-2032561	19901218	<--
	ES 2088992	T3	19961001	ES 1990-313862	19901218	<--

PRAI US 1989-452802 19891219 <--

AB A method of detg. levels of extrinsic and intrinsic **clotting factors** and **protein C** is provided which is based on the reaction rate of the obsd. **clot** formation and the 1st deriv. of the reaction rate of obsd. **clot** formation. The reaction rate of the obsd. **clot** formation in a **prothrombin** time test or an **activated** partial **thromboplastin** time assay is detd. for both test and normal **plasma** samples and the reaction rates compared. In another embodiment, the 1st deriv. of the reaction rate of the obsd. **clot** formation is detd. and the results compared. **Clot** signatures for patients with e.g. liver disease, hemophilia, and **protein C** deficiency were detd., as were those for patients undergoing coumarin therapy, etc.

ST **clotting factor** detn **clot** kinetics; **protein C** detn **clot** kinetics; **blood coagulation factor** detn **clot** kinetics

IT Hemophilia
Liver, disease or disorder
(**clotting factor** detn. in, **clot** formation reaction rate in relation to)

IT **Blood-coagulation factors**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **clot** formation reaction rate in)

IT Diagnosis
(extrinsic and intrinsic **clotting factor** and **protein C** detn. for, **clot** formation reaction rate in relation to)

IT Kinetics, enzymic
(of **clot** formation, in extrinsic and intrinsic **clotting factor** and **protein C** detn.)

IT Pharmaceuticals
(selection of, for patient, extrinsic and intrinsic **clotting factor** and **protein C** detn. for, **clot** formation reaction rate in relation to)

IT **Venoms**
(**snake**, as **protein C activator**, in **protein C** detn., **clot** formation reaction rate in relation to)

IT **Snake**
(**venom** of, as **protein C activator**, in **protein C** detn., **clot** formation reaction rate in relation to)

IT 9035-58-9, **Thromboplastin**
RL: ANST (Analytical study)
(**activated** partial, time , in extrinsic and intrinsic **clotting factor** and **protein C** detn.)

IT **9001-24-5, Blood-coagulation factor V 9001-26-7, Blood-coagulation factor II** 9001-27-8 9001-28-9, **Blood-coagulation factor** IX **9001-29-0, Blood-coagulation X** 9001-30-3, **Blood-coagulation factor** XII 9013-55-2, **Blood-coagulation factor** XI **60202-16-6, Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **clot** formation reaction rate in)

IT 91-64-5, Coumarin **9005-49-6, Heparin**, biological studies
RL: ANST (Analytical study)
(therapy with, monitoring of, **blood clotting**

factor detn. in, **clot** formation reaction rate in relation to)

L95 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:554490 HCAPLUS
DN **115:154490**
TI Method and test kit for **protein C** determination using inactivation of **factors** Va and VIIIa by **activated protein c**
IN Hassouna, Houria I.
PA Michigan State University, USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-56
ICS G01N033-86
CC **9-2** (**Biochemical Methods**)
Section cross-reference(s): 7
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9102812	A1	19910307	WO 1990-US4349	19900806 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	US 5051357	A	19910924	US 1989-396234	19890821 <--
PRAI	US 1989-396234		19890821 <--		
	US 1989-379988		19890714 <--		

AB A method and test kit for indirectly detg. **protein C** are provided. The method uses **thrombomodulin**/tissue **factor** and CaCl2 to produce **thrombin** and **activate protein C** without fibrin formation, and then allows time for the **activated protein C** to inactivate **coagulation factors** Va and VIIIa. A **plasma** sample deficient in **protein C** has a decreased **activated thromboplastin** assay **clotting** time compared to a control **plasma**. The method and test kit are useful for diagnosis of **thrombic** diseases. In addn. to a description of the assay, the issue of substrate specificity for **Agkistrodon contortrix contortrix venom**, and its **protein C-activating** component, is addressed. Std. curves for **protein C activity** are included.
ST **thrombosis** diagnosis **protein C** detn; **protein C** detn **coagulation factor** inactivation; **factor** Va inactivation **protein C** detn; VIIIa **factor** inactivation **protein C** detn; **Agkistrodon venom** substrate specificity
IT **Thrombosis**
(diagnosis of, **protein C** detn. method for)
IT **Venoms**
(**snake**, in **protein C activation** for **protein C** detn.)
IT **Blood-coagulation factors**
RL: ANST (Analytical study)
(**venom** of **Agkistrodon contortrix contortrix** effect on)
IT **Agkistrodon contortrix contortrix**
Snake
(**venom** of, in **protein C activation** for **protein C** detn.)
IT Glycoproteins, specific or class
RL: ANST (Analytical study)

(**thrombomodulins**, in **protein C** detn.)
IT **9002-05-5**, **Thromboplastin**
RL: ANST (Analytical study)
(**activated**, APTT assay, in **protein C** detn. by **coagulation factors** Va and VIIIa inactivation)
IT **9001-24-5**, **Blood-coagulation factor V** 9001-27-8
RL: PROC (Process)
(**activation** of, in **protein C** detn.)
IT **9002-04-4**, **Thrombin**
RL: ANST (Analytical study)
(**coagulation factors V** and VIII **activation** by, in **protein C** detn.)
IT **42617-41-4**, **Activated protein C**
RL: ANST (Analytical study)
(**coagulation factors** Va and VIIIa inactivation by, in **protein C** detn.)
IT **60202-16-6**, **Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **coagulation factors** Va and VIIIa inactivation in)
IT 10043-52-4, **Calcium** chloride, uses and miscellaneous
RL: USES (Uses)
(in **protein C** detn.)
IT **9005-49-6**, **Heparin**, biological studies
RL: BIOL (Biological study)
(**protein C** detn. in **plasma** of patient receiving therapeutic dose of)
IT 65522-14-7, **Blood-coagulation factor** Va 72175-66-7
RL: ANST (Analytical study)
(**protein C** detn. with inactivation of)
IT 103469-93-8, Protac
RL: ANST (Analytical study)
(substrate specificity of, **protein C** detn. in relation to)
IT **9001-26-7**, **Prothrombin**
RL: ANST (Analytical study)
(time, standardizing, in **protein C** detn.)
IT 9001-25-6, **Blood-coagulation factor** VII
RL: ANST (Analytical study)
(**venom** of **Agkistrodon contortrix contortrix** effect on)
IT **9001-29-0**, **Blood-coagulation X**
9001-30-3, **Blood-coagulation factor** XII
RL: ANST (Analytical study)
(**venom** of **Agkistrodon contortrix contortrix** effect on)

L95 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:509911 HCAPLUS
DN 115:109911
TI Comparison of test methods for the lupus **anticoagulant**: international survey on lupus **anticoagulants**-I (ISLA-1)
AU **Exner, Thomas**; Triplett, Douglas A.; Taberner, David A.; Howard, Margaret A.; Harris, E. Nigel
CS Haematol. Dep., Westmead Hosp., Sydney, Australia
SO Thromb. Haemostasis (1990), 64(3), 478-84
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
CC 9-15 (Biochemical Methods)

AB Six lyophilized **plasma** samples were sent to 20 expert labs. for assessment of lupus **anticoagulant** (LA). Four samples contained pooled LA of graded potency mixed with aged normal **plasma**. One contained LA plus cephalin phospholipid and one contained a nonspecific **venom anticoagulant**. Sixteen methods were used overall with some participants using up to 8 methods. Results were scored in regard to the known potencies of LA in the samples and other known induced defects. **Activated** partial **thromboplastin** time (APTT) tests used by most participants for preliminary screening were relatively sensitive, but nonspecific. Platelet or phospholipid neutralization procedures (PNP) appeared to be sensitive and specific but showed a nonlinear response to increased LA content. Kaolin **clotting** time (KCT) tests showed the most sensitive response to increased LA content but the weaker LA were not scored as abnormal by most labs. as the samples may have contained platelet fragments. Other commonly used tests such as the tissue **thromboplastin** inhibition (TTI) test and the dil. **Russell's viper venom** test (DRVVT) were carried out somewhat inconsistently. The variability in performance of tests in different labs. indicates that standardization of methodol. is urgently required. Generally it seemed that most **clotting** tests were bypassed by the addn. of phospholipid to a known LA-pos. sample in apparently direct proportion to their sensitivity. Sample prepn., esp. prevention of contamination with **activated** platelets is a vital preliminary part in the assay of LA.

ST lupus **anticoagulant** test method

IT Lupus erythematosus
(**anticoagulant** in, detn. of, in **blood plasma** of humans, comparison of methods for)

IT **Blood** analysis
(lupus **anticoagulant** detn. in human, comparison of methods for)

IT **Anticoagulants** and **Antithrombotics**
(lupus, detn. of, in **blood plasma** of humans, comparison of methods for)

L95 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1989:71533 HCAPLUS
DN 110:71533
TI **Functional assays** of **protein C**: **comparison** of two **snake-venom** assays with two **thrombin** assays
AU Franchi, F.; Tripodi, A.; Valsecchi, C.; Mannucci, P. M.
CS A. Bianchi Bonomi Hemophilia Thromb. Cent., Univ. Milano, Milan, Italy
SO Thromb. Haemostasis (**1988**), 60(2), 145-7
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 14

AB **Blood-coagulation factor XIV [protein C** (PC)] **activities** measured by 2 **thrombin**-based assays have been compared with those obtained by 2 assays based on **snake venom activation** of **plasma** PC followed by measurement of both the amidolytic and **anticoagulant activities** of **activated** PC. This study indicates that **snake venom** assays gave results similar to those of the **thrombin** assays in 20 healthy subjects, in 16 patients with disseminated intravascular **coagulation** disorder, and in 15 patients with congenital PC deficiency. There was, however, some degree of misclassification of normals and congenitally deficient patients, with only the **clotting snake venom** assay resulting in no misclassifications. In 15 patients stabilized on warfarin treatment and

in 17 with liver disease, the **clotting snake venom** assay gave significantly lower values than the other assays, so that it might prove to be more sensitive than the other assays to these defects.

ST **protein C** detn disease; **blood coagulation factor XIV** detn disease

IT Liver, disease or disorder
(**blood-coagulation factor XIV** detn. in human in)

IT **Blood coagulation**
(**disorder, disseminated intravascular, blood-coagulation factor XIV** detn. in human in)

IT 81-81-2, Warfarin
RL: BIOL (Biological study)
(**blood-coagulation factor XIV** detn. in human in therapy with)

IT **60202-16-6, Blood-coagulation factor XIV**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, of human in acquired and congenital deficiencies, comparison of **snake venom** and **thrombin** assays for)

L95 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1988:545019 HCAPLUS
DN 109:145019
TI Fast **functional assay** of **protein C** in whole **plasma** using a **snake venom activator**: evaluation in patients with congenital and acquired **protein C** deficiencies
AU Takahashi, Hoyu; Hanano, Masaharu; Tatewaki, Wataru; Shibata, Akira
CS Sch. Med., Niigata Univ., Asahimachi, Japan
SO Clin. Chim. Acta (**1988**), 175(3), 217-25
CODEN: CCATAR; ISSN: 0009-8981
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 14
AB Both **anticoagulant** and amidolytic **activities** of **protein C** (PC) were measured using a **snake venom activator** in patients with hereditary PC deficiency, disseminated intravascular **coagulation** (DIC), and under stabilized warfarin therapy. The results were compared with those obtained by an ELISA. PC levels measured by different functional and immunol. assays were very close in patients with hereditary PC deficiency and DIC. In patients under stable oral **anticoagulant** therapy, there was no detectable difference between amidolytic **activity** and antigen levels of PC in each patient **plasma**, whereas a decrease in **anticoagulant activity** was much more pronounced. The present **activity** assays measure PC specifically, and the **snake venom activator** can **activate** both carboxylated and hypocarboxylated forms of PC, but only **anticoagulant** assay can evaluate the physiol. PC function in vitamin K-deficient states.

ST **plasma protein C** detn disease; **coagulation factor XIV** detn **plasma**; amidolytic assay **protein C plasma**; **anticoagulant protein C plasma**; immunoassay **protein C plasma**

IT **Agkistrodon contortrix contortrix**
(**protein C activator** of **venom** of, in **protein C** functional **activity** detn. in human **blood plasma**)

IT **Venoms**
(**protein C activator** of, of **Agkistrodon contortrix contortrix**, in **protein C** functional **activity** detn. in human **blood plasma**)
IT **Blood coagulation**
(**disorder, disseminated intravascular, protein C** functional assays in human **blood plasma** in, ELISA in relation to)
IT **60202-16-6, Blood-coagulation factor XIV**
RL: BIOL (Biological study)
(**anticoagulant** and amidolytic **activities** of, detn. of, in human **blood plasma** in health and disease with **snake venom activator**, ELISA in relation to)
IT **9001-26-7, Blood-coagulation factor II 9001-29-0, Blood-coagulation factor X**
RL: BIOL (Biological study)
(of **blood plasma** of human, **protein C** in relation to, in warfarin therapy)
IT 81-81-2, Warfarin
RL: BIOL (Biological study)
(therapy with, **protein C** functional assays in human **blood plasma** in)

L95 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1988:146143 HCAPLUS
DN 108:146143
TI Characterization and some properties of the **protein C activator** from **Agkistrodon contortrix contortrix venom**
AU **Exner, Thomas**; Vaasjoki, Riita
CS Haematol. Dep., Westmead Hosp., Westmead, Australia
SO Thromb. Haemostasis (**1988**), 59(1), 40-4
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 12
AB The **protein C activator** (PCA) detectable in the **venom** of **A. contortrix** contortrix (Southern **copperhead**) by specific immunochromometric assay and **anticoagulant activity** was isolated and partially characterized. Chromatog. of the crude **venom** on SP-Sephadex followed by Con A Sepharose and finally on hydroxylapatite was necessary to achieve an electrophoretically pure product. The isolated PCA is a single-chain glycoprotein with a strong pos. charge and an apparent mol. wt. of 36,000. It had an immediate inhibitory effect on the **activated** partial **thromboplastin** time (APTT) of normal **plasma** with no noticeable effect on the **prothrombin** time. Its effect on the APTT was dependent on **protein C** and appeared to interfere with the contact mechanism rather than with **factors V** and VIII. It had enzymic **activity** on some tripeptide chromogenic substrates sensitive to **thrombin** and kallikrein. When mixed with normal **plasma** it generated **activity** on substrates sensitive to **activated protein C** and should be useful for studies of **protein C**.
ST **Agkistrodon venom protein C activator; snake venom protein C activator**

IT **Blood-coagulation factors**
RL: BIOL (Biological study)
(**protein C activator** of Southern **copperhead venom** effect on)
IT **Blood coagulation**
(**protein C activator** of Southern **copperhead venom** inhibition of)
IT **Agkistrodon contortrix contortrix**
(**protein C activator** of **venom** of, isolation and characterization of)
IT **Venoms**
(**protein C activator** of, of Southern **copperhead**, isolation and characterization of)
IT Kininogens
RL: BIOL (Biological study)
(high-mol.-wt., **protein C activator** of Southern **copperhead venom** effect on)
IT **60202-16-6, Blood-coagulation factor XIV**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**activator**, of **venom** of Southern **copperhead**, isolation and characterization of)
IT 9001-27-8, **Blood-coagulation factor** VIII, complex 9001-28-9, **Blood-coagulation factor** IX 9001-30-3, **Blood-coagulation factor** XII 9013-55-2, **Blood-coagulation factor** XI 9055-02-1, Prekallikrein
RL: BIOL (Biological study)
(**protein C activator** of Southern **copperhead venom** effect on)

L95 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:529568 HCAPLUS
DN **107:129568**
TI **Protein C**: an automated **activity** assay
AU Oedegaard, O. R.; Try, K.; Andersson, T. R.
CS Dep. Clin. Chem., Aker Sykehus, Oslo, Norway
SO Haemostasis (**1987**), 17(3), 109-13
CODEN: HMTSB7; ISSN: 0301-0147
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 14
AB **Protein C** in citrated **plasma** is specifically **activated** by the **snake venom** deriv. Protac, and the **activator** is used in a simple, automated assay method. The **activation** is completed in <120 s and isolation of **protein C** from its inhibitor before **activation** is not necessary. The **activated protein C** is detd. with the chromogenic substrate S-2366. Therapeutic concns. of **heparin** in the test sample do not influence the result. A strong pos. correlation to immunoassay of **protein C** is found. Three cases of probable hereditary **protein C** deficiency belonging to the same family were discovered during the study.
ST **protein C** detn **plasma**
IT **Blood coagulation**
(disorder, **protein C** deficiency in human)
IT **60202-16-6, Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in human **plasma**, automated)
IT 72194-57-1, S-2366 103469-93-8, Protac
RL: BIOL (Biological study)
(in **protein C** automated assay, in human

blood plasma)

L95 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:435685 HCAPLUS
DN **107:35685**
TI Quantitative **determination** of **protein C** and **activator** preparation for its implementation
IN Stocker, Kurt F.; Svendsen, Lars G.
PA Pentapharm A.-G., Switz.
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM C12Q001-38
ICA C12Q001-56; G01N033-86; A61K035-38; G01N033-68
CC 7-1 (Enzymes)
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 203509	A2	19861203	EP 1986-106881	19860521	<--
	EP 203509	A3	19881005			
	EP 203509	B1	19910403			
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE					
	AU 8657369	A1	19861204	AU 1986-57369	19860513	<--
	AU 605462	B2	19910117			
	DK 8602248	A	19861130	DK 1986-2248	19860514	<--
	DK 165199	B	19921019			
	DK 165199	C	19930301			
	IL 78829	A1	19900831	IL 1986-78829	19860519	<--
	AT 62274	E	19910415	AT 1986-106881	19860521	<--
	NO 8602118	A	19861201	NO 1986-2118	19860528	<--
	NO 166303	B	19910318			
	NO 166303	C	19910626			
	ES 555428	A1	19871201	ES 1986-555428	19860528	<--
	CA 1286223	A1	19910716	CA 1986-510137	19860528	<--
	JP 61280298	A2	19861210	JP 1986-122398	19860529	<--
	JP 07036760	B4	19950426			
	ES 557670	A1	19880716	ES 1987-557670	19870814	<--
	ES 557670	A5	19880809			

PRAI	CH 1985-2267	19850529	<--
	CH 1985-4135	19850925	<--
	CH 1985-5087	19851128	<--
	EP 1986-106881	19860521	<--

AB **Protein C** is detd. in **plasma** or other samples by **activation** with **snake venom**, followed by **incubation** of the **activated protein C** (i.e. proteolytically **active** protein **Ca**) with a chromogenic oligopeptide substrate R2-D-NHCH[(CH2)NHR3]CO-L-Pro-L-Arg-R1 [R1 = NHC6H3NO2-4, NHC10H7; R2 = H, C2-6 alkanoyl, alkoxycarbonyl, C1-2 alkylsulfonyl, (substituted) benzoyl, (substituted) benzyloxycarbonyl, etc.; R3 = R2, amidino, tosylamidino; n = 3,4] and photometric detn. of the cleavage products. The **venom**, from **Agkistrodon** contortix, contains a **protein C activator** which is useful as an **antithrombotic** . This **activator** was purified from **venom** by chromatog. on DEAE-Sephadex A-50 and used for detn. for **protein C** in citrated human **plasma** with D-cyclohexylglycyl-L-prolyl-L-arginine p-nitroanilide-2AcOH as substrate for the protein C2 formed. The **protein C activated** from **venom** did not **coagulate** fibrinogen, did not lyse fibrin, and was not inhibited by **antithrombin** III, **heparin**, hirudin, or aprotinin. It had a mol. wt. of about 39,000, and isoelec.

point of 3.0, and a carbohydrate content of 20%.
ST **protein C** detn **plasma; Agkistradon venom protein C activator; snake venom protein C activator**
IT Peptides, uses and miscellaneous
RL: USES (Uses)
(chromogenic, for **protein C** detn., **activator** from **snake venom** in relation to)
IT **Agkistrodon contortrix**
Snake
(**protein C activator** of **venom** of)
IT **Venoms**
(**protein C activator** of, of **snake**)
IT Escherichia coli
Microorganism
Saccharomyces cerevisiae
(**protein C** detn. in genetically engineered, **activator** from **snake venom** in)
IT Animal tissue culture
Organ
(**protein C** detn. in, **activator** from **snake venom** in)
IT **Blood analysis**
(**protein C** detn. in, of human and other mammals, **activator** from **snake venom** in)
IT 86890-95-1 88927-41-7 102565-94-6 108963-64-0 108963-66-2 108963-67-3 108963-68-4 108963-70-8 108963-71-9 108963-72-0 108963-74-2 108998-14-7
RL: BIOL (Biological study)
(as chromogenic substrate, in **protein C** detn., **activator** from **snake venom** in relation to)
IT **60202-16-6, Blood-coagulation factor XIV**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **activator** from **snake venom** in)
IT **42617-41-4, Blood-coagulation factor XIVa**
RL: FORM (Formation, nonpreparative)
(formation of, **protein C activator** from **snake venom** in)

L95 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:191586 HCAPLUS
DN 106:191586
TI **Measurement** of **protein C** in **plasma** - a fully automated assay
AU McCall, F.; Conkie, J. A.; Walker, I. D.; Davidson, J. F.
CS Dep. Haematol., R. Infirm., Glasgow, UK
SO Thromb. Res. (**1987**), 45(5), 681-5
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 1, 14
AB The assay for vitamin K-dependent **protein C** (**coagulation factor XIV**), which uses a rapid **activator** (Protac C) of **protein C** derived from the **venom** of the **copperhead snake**, was simple and reliable. Using a Gilford 203-S clin. analyzer, the assay was fully automated. It was not subject to the constraints of isolation of

protein C from **plasma** by absorption and elution nor of inhibiting excess **protein C activator**. The assay required only 25 .mu.L test **plasma** and performed at 70 tests/h with good precision and sensitivity; carry-over was within acceptable limits. No **factor Xa** or **thrombin** generation occurred. In both normal controls and untreated patients, good agreement was obtained for **protein C** as detd. by the automated Protac C method and the ELISA procedure. In oral **anticoagulant**-treated patients, however, there was less agreement between the 2 methods as (1) the correlation was lower than that found in the other 2 groups, and (2) **activity** levels of **protein C** were generally lower than the antigen levels (mean values 29% vs. 48%, resp.). Therefore, it seems likely that the method using Protac C **activator** measures only the .gamma.-carboxylated form of **protein C**.

ST **protein C** detn **thrombosis**; **blood coagulation factor XIV** detn automated; Protac C **coagulation factor XIV** detn

IT **Thrombosis**
(**blood-coagulation factor XIV** automated amidolytic detn. in human in)

IT **Anticoagulants** and **Antithrombotics**
(oral, **blood-coagulation factor XIV** amidolytic detn. in human **plasma** response to)

IT **60202-16-6, Blood-coagulation factor XIV**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, of human **plasma**, fully automated amidolytic)

IT 103469-93-8
RL: BIOL (Biological study)
(in **blood-coagulation factor XIV** automated amidolytic detn. in human **plasma**)

L95 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1986:456677 HCAPLUS
DN 105:56677
TI **Determination** of **protein C** in **plasma**
AU Loebermann, H.; Kolde, H. J.; Deubel, R.; Peter, R.; Tourte, E.; Becker, U.
CS Res. Lab., Behringwerke AG, Marburg/Lahn, D-3550, Fed. Rep. Ger.
SO Behring Inst. Mitt. (**1986**), 79, 112-20
CODEN: BHIMA2; ISSN: 0301-0457
DT Journal
LA English
CC 7-1 (Enzymes)
AB Three new methods to characterize the function of vitamin K-dependent **protein C** (**blood-coagulation factor XIV**) in **plasma** are described and compared to established procedures. Two methods use a **snake venom**-derived specific **protein C activator** which allows rapid, sensitive, and standardizable assays in **plasma** without sample pretreatment. The other technique is 2-dimensional immunoelectrophoresis in the presence of **Ca2+** or EDTA.

ST **blood coagulation factor XIV** detn **plasma**; vitamin K **protein C** detn **plasma**

IT **60202-16-6**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in human **blood plasma**, comparison of methods for)

L95 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1986:47533 HCAPLUS
DN 104:47533
TI Detection of specific proenzyme **activators** in **snake venoms** by a new immunoabsorbant-chromogenic substrate **method**
AU **Exner, Thomas**; Cotton, Beth; Howden, Merlin
CS Haematol. Dep., Westmead Hosp., Westmead, NSW 2145, Australia
SO Biochim. Biophys. Acta (**1985**), 832(3), 351-6
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
CC 7-1 (Enzymes)
AB In sep. expts., antibodies to plasminogen, **blood-coagulation factor X**, and **protein C** were applied to microtiter trays as commonly used in ELISA. After **incubation** with dil. normal human **plasma** as a source of the corresponding proenzyme antigen, the wells were exposed to dilns. of various **snake venoms**. After thorough washing, the microtiter tray wells were tested overnight with chromogenic tripeptide substrates known to be relatively specific for the **activated** forms of the above **factors**, i.e., plasmin, **factor Xa**, and **activated protein C**. The immunochromometric assay described detected 2 new **activators** of **protein C** in **Agkistrodon piscivorus** and **A. contortrix venoms** and a new **factor X activator** in A. rhodostoma **venom**. Gel filtration of the latter **venom** indicated that the **factor X activator** eluted with high mol. wt., was clearly distinct from the peak fibrinogen **clotting activity** (Ancrod), and appeared to have no **procoagulant activity**. Although several Bothrops **venoms** appeared to contain plasminogen **activator** by this technique, the obsd. strong chromogenic **activity** was obsd. in microtiter wells independently of plasminogen and represented nonspecific amidase **activity**.
ST proenzyme **activator** detection **snake venom**; **Agkistrodon venom** proenzyme **activator** detection; **protein C activator** detection **Agkistrodon venom**; **blood factor X activator** detection **Agkistrodon**
IT Zymogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**activators**, in **snake venom**, detection of)
IT Bothrops
(amidase in **venom** of, detection of)
IT **Agkistrodon** rhodostoma
(**blood-coagulation factor X activator** in **venom** of)
IT **Snake**
(proenzyme **activators** in **venoms** of, detection of)
IT **Venoms**
(proenzyme **activators** in, of **snakes**, detection of)
IT **Agkistrodon contortrix**
Agkistrodon piscivorus
(**protein C activator** in **venom** of)
IT **9001-29-0 60202-16-6**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**activators**, in **snake venoms**, detection of)
IT 9012-56-0
RL: PROC (Process)

(in **venom** of Bothrops, detection of)

L95 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1974:459805 HCAPLUS
DN 81:59805
TI Biochemical properties of a **coagulant** enzyme from **Agkistrodon** rhodostoma **venom**
AU **Exner, Thomas**
CS Univ. Waterloo, Waterloo, Ont., Can.
SO (1973) No pp. given Avail.: Natl. Libr. Canada, Ottawa, Ont
From: Diss. Abstr. Int. B 1974, 34(10), 4817-18
DT Dissertation
LA English
CC 7-2 (Enzymes)
AB Unavailable
ST **coagulant** enzyme **Agkistrodon venom**
IT Enzymes
RL: BIOL (Biological study)
(**coagulant**, of **Agkistrodon** rhodostoma **venom**
)
IT **Venoms**
(of **Agkistrodon** rhodostoma, **coagulant** enzyme of)
IT **Agkistrodon** rhodostoma
(**venom** of, **coagulant** enzyme of)

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L63 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:578846 HCAPLUS
DN 115:178846
TI Method and kit for determining the endogenous thrombin potential of plasma and blood and for pharmaceutical analysis
IN Hemker, Hendrik Coenraad; Beguin, Suzette Lucette
PA Neth.
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C12Q001-56
CC 9-2 (Biochemical Methods)
Section cross-reference(s): 1, 7
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 420332	A2	19910403	EP 1990-202509	19900921
	EP 420332	A3	19910508		
	EP 420332	B1	19950426		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	NL 8902406	A	19910416	NL 1989-2406	19890927
	AT 121792	E	19950515	AT 1990-202509	19900921
	ES 2072970	T3	19950801	ES 1990-202509	19900921
	JP 03236798	A2	19911022	JP 1990-260273	19900927
	JP 3137261	B2	20010219		
	US 5192689	A	19930309	US 1990-588924	19900927
PRAI	NL 1989-2406	A	19890927		

AB A method for detg. the endogenous thrombin potential (ETP) is described which shows how much and for what length of time thrombin has been active in a sample of clotting blood or plasma. The ETP can be used for detg. the effectiveness of treatment with antithrombotics of any type. The ETP detn. comprises adding to the sample a thrombin substrate, an activator of thrombin formation, a prepn. of protease inhibitor and, if desired, a pharmaceutical for anal. The thrombin substrate is preferably selected to

not completely consume the amt. of thrombin generated in the sample, to have a rate of conversion of the substrate which is proportional to the amt. of thrombin present and to have a measurable conversion product resulting from the conversion by thrombin. Detn. of the amt. of conversion product leads to detn. of the ETP. The choice of activator dets. whether the effect is measured on the intrinsic or extrinsic clotting system, making it possible to det. the effect of the pharmaceutical on various parts of the clotting mechanism. Defibrinated plasma samples contg. various concns. of low-mol. wt. heparin (Fraxiparine) were mixed with buffer contg. CH3OCO-Gly-Pro-Arg-p-nitroanilide.HCl, thromboplastin, CaCl2, and antithrombin III. Optical d. at 405 nm was measured 6 min later.

ST blood thrombin potential detn; pharmaceutical analysis blood thrombin potential

IT Blood analysis
(endogenous thrombin potential detn. in)

IT Pharmaceutical analysis
(endogenous thrombin potential detn. in plasma or blood in)

IT Anticoagulants and Antithrombotics
(endogenous thrombin potential of plasma or blood response to)

IT Poisons
(of Oxyuranus scutellatis, in endogenous thrombin potential detn. in plasma or blood)

IT Oxyuranus scutellatus
(poison of, in endogenous thrombin potential detn. in plasma or blood)

IT Fibrins
RL: ANST (Analytical study)
(polymn., inhibition of, in endogenous thrombin potential detn. in plasma or blood)

IT Spectrochemical analysis
(fluorometric, endogenous thrombin potential detn. in plasma or blood by)

IT Peptides, compounds
RL: ANST (Analytical study)
(oligo-, arginine-contg., conjugates, with detectable leaving group, as substrate in endogenous thrombin potential detn. of plasma or blood)

IT Peptides, compounds
RL: ANST (Analytical study)
(oligo-, conjugates, with detectable leaving group, as substrate in endogenous thrombin potential detn. of plasma or blood)

IT Spectrochemical analysis
(spectrophotometric, endogenous thrombin potential detn. in plasma or blood by)

IT 9000-94-6, Antithrombin **136535-64-3**
RL: ANST (Analytical study)
(as protease inhibitor in endogenous thrombin potential detn. of plasma or blood)

IT 901-47-3 60457-00-3, S2222 136552-31-3
RL: ANST (Analytical study)
(as substrate in endogenous thrombin potential detn. of plasma or blood)

IT 9002-04-4, Thrombin
RL: PRP (Properties)
(blood or plasma potential of, detn. of)

IT 104521-37-1, Fraxiparine
RL: ANST (Analytical study)
(endogenous thrombin potential of defibrinated plasma response to)

IT 24967-94-0, Dermatan sulfate 9005-49-6, Heparin, biological studies
RL: ANST (Analytical study)
(endogenous thrombin potential of plasma or blood response to)

IT 618-39-3, Benzamidine 9002-05-5, Thromboplastin 136552-32-4
7440-70-2, Calcium, biological studies 8001-27-2, Hirudin 10043-52-4, Calcium chloride, biological studies

```
     RL: ANST (Analytical study)
        (in endogenous thrombin potential detn. of plasma or blood)
IT   9001-26-7, Prothrombin
     RL: ANST (Analytical study)
        (thrombin generation and detn. from, prolonged anticlotting treatment
        effect on)


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L63  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2002 ACS
IT   136535-64-3
     RL: ANST (Analytical study)
        (as protease inhibitor in endogenous thrombin potential detn. of plasma
        or blood)
RN   136535-64-3  HCAPLUS
CN   Antithrombin, mixt. with heparin cofactor II (9CI)  (CA INDEX NAME)

     CM   1

     CRN  81604-65-1
     CMF  Unspecified
     CCI  MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

     CM   2

     CRN  9000-94-6
     CMF  Unspecified
     CCI  PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***


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     (FILE 'HOME' ENTERED AT 07:32:18 ON 13 MAY 2002)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 07:32:46 ON 13 MAY 2002
               E PROTEIN C/CN
L1           1 S E3
               E ACTIVATED PROTEIN C/CN
L2           1 S E3
               E BLOOD-COAGULATION FOACTOR XA/CN
               E BLOOD-COAGULATION FACTOR XA/CN
L3           1 S E3
               E ANTITHROMBIN III/CN
L4           1 S E3
               E HEPARIN COFACTOR 2/CN
L5           1 S E6
L6           2 S 9000-94-6/CRN
L7           1 S 81604-65-1/CRN
L8           1 S L6 AND L7
               E BLOOD-COAGULATION FACTOR X/CN
L9           1 S E3
               E PROTHROMBIN/CN
L10          1 S E3
               E THROMBIN/CN
L11          1 S E3
               E BLOOD-COAGULATION FACTOR V/CN
L12          1 S E3
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L13           2 S (HEPARIN OR HEPARIN, SODIUM SALT)/CN
L14           1 S DERMATAN/CN
L15           1 S DEXTRAN SULPHATE/CN

     FILE 'HCAPLUS' ENTERED AT 07:39:58 ON 13 MAY 2002
                 E EXNER T/AU
L16          54 S E3-E5
                 E GRADIPORE/PA,CS
L17          33 S E3-E18
L18          80 S L16,L17
                 E OW99-AU69/AP,PRN
                 E WO99-AU69/AP,PRN
L19           1 S E3,E4
L20           1 S L18 AND L19

     FILE 'REGISTRY' ENTERED AT 07:44:29 ON 13 MAY 2002
L21           1 S 14127-61-8
L22           1 S 28728-55-4
L23           1 S 166799-93-5

     FILE 'HCAPLUS' ENTERED AT 07:45:52 ON 13 MAY 2002
                 E VENOM/CW
L24        9457 S E4
                 E VENOM/CT
                 E E7+ALL
L25        9273 S E3+NT
L26       19658 S E3,E5/BI
L27        7518 S SNAKE(L)VENOM?
L28       19690 S L24-L27
                 E AGKISTRODON/CT
                 E E3+ALL
L29         518 S E6+NT
L30        1268 S E6-E27/BI
                 E AGKISTRODON
L31        1277 S E1-E14
L32         243 S (AGKISTRO? OR A)()(CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MO
L33         227 S AGKISTRO? (L) (CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MOCCAS
L34       19855 S L28-L33
                 E VIPER/CT
                 E E4+ALL
L35           2 S E3,E4
                 E E28+ALL
L36         262 S E7+NT
L37         369 S E7-E12/BI
                 E E6+ALL
L38         615 S E6+NT
L39        1124 S E6-E35/BI
                 E VIPER
L40        2387 S E3,E4,E7,E8,E9,E10,E11
L41         447 S E13-E17,E22,E23,E24
                 E NOTECHIS/CW
L42         104 S E3
                 E NOTECHIS/CT
                 E E3+ALL
L43         104 S E6+NT
L44         162 S E6-E17/BI
                 E PSEUDONAJA/CT
                 E E3+ALL
L45          38 S E6+NT
L46          54 S E6-E12/BI
                 E OXYURANUS/CT
                 E E5+ALL
L47          77 S E6+NT
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L48          122 S E6-E10/BI
L49        20335 S L34-L48
L50          976 S RUSSEL?(L)(SNAKE OR VIPER?)
L51          156 S COPPERHEAD OR COPPER HEAD
L52        20373 S L49-L51
L53           11 S L18 AND L52
                 E BLOOD COAGULATION/CT
                 E E3+ALL
L54        12573 S E7+NT
                 E BLOOD CLOT/CT
                 E E6+ALL
L55          483 S L52 AND L54
L56         2295 S L52 AND (?COAGUL? OR CLOT?)
L57         2295 S L55,L56
L58          168 S L52 AND (L1 OR PROTEIN C OR FACTOR XIV)
L59          158 S L52 AND (L2 OR PROTEIN C (L) ACTIV? OR FACTOR XIVA)
L60          157 S L58 AND L59
L61           42 S L60 AND (L3 OR FACTOR XA OR FACTOR X(L)ACTIV?)
L62            0 S L60 AND L8
L63            1 S L8
L64            1 S L60 AND (L4 OR ANTITHROMBIN III) AND (L5 OR HEPARIN (L) COFAC
L65          103 S L60 AND (L9 OR FACTOR X OR L10 OR PROTHROMBIN OR FACTOR II OR
L66           24 S L60 AND (L21 OR CALCIUM(L)ION OR CA2# OR CA(L)ION)
L67           19 S L60 AND (L13 OR L14 OR L15 OR HEPARIN OR DERMATAN OR DEXTRAN(
L68           18 S L60 AND (L23 OR FACTOR(L)V (L) LEIDEN)
L69           76 S L61,L66-L68
L70           62 S L69 AND L65
L71           22 S L70 AND 9/SC
L72           16 S L69 AND BLOOD ANALYSIS/CT
L73            8 S L71 AND L72
L74            8 S L73 AND L24-L73
                 SEL DN 3 5 6
L75            5 S L74 NOT E1-E3
L76          128 S L60 AND (PD<=19980202 OR PRD<=19980202 OR AD<=19980202)
L77           29 S L76 AND (BIOCHEM?(L)METHOD?)/SC,SX
L78           26 S L77 AND L61-L75
L79           68 S L76 AND L61-L75 NOT L77
L80           17 S L79 AND (SCREENING OR KIT OR FUNCTIONAL ASSAY OR COMPARISON O
L81            2 S L79 AND PROTAC/TI
L82            6 S L79 AND BLOOD ANALYSIS/CT
                 SEL DN 5 6
L83            4 S L82 NOT E4-E5
L84           13 S L80 NOT L81-L83
                 SEL DN 3 7 12 13
L85            9 S L84 NOT E6-E9
L86           31 S L20,L53,L63,L64,L75,L81,L83,L85
L87           59 S L69 AND L76
L88           46 S L87 NOT L86
                 SEL DN 4 6 9 15 23 27 28 38 39
L89            9 S L88 AND E10-E18
L90           18 S L85,L89
L91           29 S L53,L90
L92           29 S L91 AND (?COAGUL? OR CLOT? OR FACTOR OR BLOOD OR PLASMA OR SE
L93           11 S L91 AND (RUSSEL? OR VIPER? OR PSEUDON? OR TEXTIL? OR NOTECH?
L94           29 S L92,L93 AND L16-L20,L24-L93
                 SEL DN 20
L95           28 S L94 NOT E19

     FILE 'HCAPLUS' ENTERED AT 09:33:59 ON 13 MAY 2002

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FILE 'BIOSIS' ENTERED AT 09:48:20 ON 13 MAY 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 8 May 2002 (20020508/ED)

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L109 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:61534 BIOSIS
DN **PREV200200061534**
TI Apparatus and method for detecting coagulation in blood samples.
AU **Exner, T.**
CS Gordon Australia
ASSIGNEE: GRADIPORE LIMITED
PI US 5601995 Feb. 11, 1997
SO Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 11, 1997) Vol. 1195, No. 2, pp. 1164.
ISSN: 0098-1133.
DT **Patent**
LA English
NCL 435013000
CC Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
Methods, Materials and Apparatus, General - Laboratory Methods *01004
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Methods and Techniques
IT Miscellaneous Descriptors
ANALYTICAL TECHNIQUES; BLOOD SAMPLE; COAGULATION; METHODS

L109 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:451086 BIOSIS
DN **PREV200000451086**
TI Activated protein C resistance test.
AU **Exner, Thomas (1)**
CS (1) Gordon Australia
ASSIGNEE: Gradipore Limited, North Ryde, Australia
PI US 6051434 April 18, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 18, 2000) Vol. 1233, No. 3, pp. No pagination. e-file.
ISSN: 0098-1133.
DT **Patent**
LA English
AB The method for determining functional activity of protein C in a human plasma sample includes incubating the human plasma sample with exogenous reagents that activate factor V and a common pathway of the blood coagulation mechanism through factor X, with activated exogenous protein C and with components that are necessary for efficient clotting of the human plasma sample, or incubating the human plasma sample with exogenous reagents that induce the presence of thrombin in a factor V dependent manner, with activated exogenous protein C and with components that are necessary for efficient clotting of the human plasma sample; monitoring a reaction indicative of a potential rate of coagulation of the plasma sample and comparing the resulting potential rate of coagulation with an equivalent rate for normal patient, or comparing the resulting potential rate of coagulation with an equivalent rate determined for the plasma sample in the absence of activated exogenous protein C; and determining the functional activity of the free protein C from this comparison.
NCL 436069000
BC Hominidae 86215

IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques; Blood and Lymphatics (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics
IT Chemicals & Biochemicals
factor V; factor X; protein C
IT Methods & Equipment
activated protein C resistance test: analytical method
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 9001-29-0 (FACTOR X)
60202-16-6 (PROTEIN C)

L109 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:146080 BIOSIS
DN **PREV199900146080**
TI Methods for subtyping lupus anticoagulants.
AU **Exner, T. (1)**
CS (1) Haemostasis Res. Lab., Gradipore Ltd., PO Box 1865, Macquarie Cent., North Ryde, NSW 2113 Australia
SO Lupus, (1998) Vol. 7, No. SUPPL. 2, pp. S103-S106.
Meeting Info.: 8th International Symposium on Antiphospholipid Antibodies Sapporo, Japan October 6-9, 1998
ISSN: 0961-2033.
DT Conference
LA English
CC Immunology and Immunochemistry - General; Methods *34502
Biochemical Studies - General *10060
Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Immune System (Chemical Coordination and Homeostasis)
IT Chemicals & Biochemicals
beta-2-glycoprotein 1: plasma; lupus anticoagulants: beta-2-glycoprotein 1-dependence, prothrombin cofactor-dependence, subtypes; prothrombin: plasma
IT Miscellaneous Descriptors
activated partial thromboplastin time: clotting test; dilute **Russell's viper venom** time: clotting test; kaolin clotting time: clotting test; Meeting Abstract; Meeting Paper
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 9001-26-7 (PROTHROMBIN)
9002-05-5Q (THROMBOPLASTIN)
9035-58-9Q (THROMBOPLASTIN)
72162-96-0Q (THROMBOPLASTIN)

L109 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:60955 BIOSIS
DN **PREV199800060955**

TI Sensitivity of **Russells viper venom** tests to factor VIII inhibitors.
AU **Exner, T.**; Dickeson, L. E.
CS Gradipore Res. Lab., North Ryde, NSW 2113, Sydney Australia
SO Blood, (**Nov. 15, 1997**) Vol. 90, No. 10 SUPPL. 1 PART 2, pp. 93B. Meeting Info.: Thirty-ninth Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997 The American Society of Hematology . ISSN: 0006-4971.
DT Conference
LA English
CC **Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001**
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10502
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation)
IT Diseases
hemophilia: blood and lymphatic disease, genetic disease
IT Chemicals & Biochemicals
factor VIII inhibitors: discrimination; lupus anticoagulants: discrimination
IT Methods & Equipment
Russels viper venom-based clotting test: determination method, sensitivity
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 9001-27-8Q (FACTOR VIII)
109319-16-6Q (FACTOR VIII)
113189-02-9Q (FACTOR VIII)

L109 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:505111 BIOSIS
DN **PREV199598510161**
TI Diagnostic methodologies for circulating anticoagulants.
AU **Exner, Thomas**
CS GRADIPORE, Riverside Corp. Park, 35-105 Delhi Rd., PO Box 1865, Macquarie Cent., North Ryde 2113 Australia
SO Thrombosis and Haemostasis, (1995) Vol. 74, No. 1, pp. 338-344. ISSN: 0340-6245.
DT General Review
LA English
CC Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Lipids 10066
Biochemical Studies - Carbohydrates *10068
Pathology, General and Miscellaneous - Diagnostic *12504
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002

Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Reproductive System - Pathology *16506
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Hematology (Human Medicine, Medical Sciences); Metabolism; Pathology; Reproductive System (Reproduction)
IT Chemicals & Biochemicals
THROMBOPLASTIN
IT Miscellaneous Descriptors
ACQUIRED THROMBOTIC DISORDER; ACTIVATED PARTIAL THROMBOPLASTIN TIME; DILUTE **RUSSELL**'S **VIPER VENOM** TIME; KAOLIN CLOTTING TIME; PHOSPHOLIPID-INTERFERING ANTIBODY; RECALCIFICATION CLOTTING TIME; RECURRENT SPONTANEOUS ABORTION; TEXATRIN AND TAIPAN **VENOM** TEST; TISSUE THROMBOPLASTIN INHIBITION TEST
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 9002-05-5Q (THROMBOPLASTIN)
9035-58-9Q (THROMBOPLASTIN)
72162-96-0Q (THROMBOPLASTIN)

L109 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:310535 BIOSIS
DN **PREV199497323535**
TI Some recent developments with lupus anticoagulants.
AU **Exner, T.**
CS Haemostasis Reference Lab., Westmead Hosp., Sydney, NSW 2145 Australia
SO Blood Coagulation & Fibrinolysis, (1994) Vol. 5, No. 2, pp. 281-289.
ISSN: 0957-5235.
DT General Review
LA English
AB Lupus anticoagulants (LA) have been defined as phospholipid-interfering antibodies. Testing for them has become a frequently requested procedure in coagulation laboratories and new methods have recently become available. Activated partial thromboplastin time (aPTT) reagents with reduced levels or different types of phospholipid provide high sensitivity. Correction procedures resistant to heparin and based on aPTT and dilute **Russell's viper venom** time
(DRVVT) tests with added hexagonal phase phospholipids have improved the specificity of testing. Simplified tests based on **venom**
activators of factor X and prothrombin improve the reliability of LA testing and may facilitate the further categorization of circulating anticoagulants. Recent studies on the mechanism of LA derived from various patients have confirmed their heterogeneity, principally in the protein cofactors involved in their interactions with phospholipids. Perhaps one-third of LA require beta-2-glycoprotein 1 to exert an anticoagulant effect. The remainder may require human prothrombin as suggested from studies with reconstituted clotting factor systems.
CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
BC Hominidae *86215

IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Hematology (Human Medicine, Medical Sciences); Metabolism
IT Miscellaneous Descriptors
ANTIPHOSPHOLIPID ANTIBODY; THROMBOSIS
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

=> d his

(FILE 'HOME' ENTERED AT 07:32:18 ON 13 MAY 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 07:32:46 ON 13 MAY 2002
E PROTEIN C/CN
L1 1 S E3
E ACTIVATED PROTEIN C/CN
L2 1 S E3
E BLOOD-COAGULATION FOACTOR XA/CN
E BLOOD-COAGULATION FACTOR XA/CN
L3 1 S E3
E ANTITHROMBIN III/CN
L4 1 S E3
E HEPARIN COFACTOR 2/CN
L5 1 S E6
L6 2 S 9000-94-6/CRN
L7 1 S 81604-65-1/CRN
L8 1 S L6 AND L7
E BLOOD-COAGULATION FACTOR X/CN
L9 1 S E3
E PROTHROMBIN/CN
L10 1 S E3
E THROMBIN/CN
L11 1 S E3
E BLOOD-COAGULATION FACTOR V/CN
L12 1 S E3
L13 2 S (HEPARIN OR HEPARIN, SODIUM SALT)/CN
L14 1 S DERMATAN/CN
L15 1 S DEXTRAN SULPHATE/CN

FILE 'HCAPLUS' ENTERED AT 07:39:58 ON 13 MAY 2002
E EXNER T/AU
L16 54 S E3-E5
E GRADIPORE/PA,CS
L17 33 S E3-E18
L18 80 S L16,L17
E OW99-AU69/AP,PRN
E WO99-AU69/AP,PRN
L19 1 S E3,E4
L20 1 S L18 AND L19

FILE 'REGISTRY' ENTERED AT 07:44:29 ON 13 MAY 2002
L21 1 S 14127-61-8
L22 1 S 28728-55-4
L23 1 S 166799-93-5

FILE 'HCAPLUS' ENTERED AT 07:45:52 ON 13 MAY 2002
E VENOM/CW

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L24          9457 S E4
                  E VENOM/CT
                  E E7+ALL
L25          9273 S E3+NT
L26         19658 S E3,E5/BI
L27          7518 S SNAKE(L)VENOM?
L28         19690 S L24-L27
                  E AGKISTRODON/CT
                  E E3+ALL
L29           518 S E6+NT
L30          1268 S E6-E27/BI
                  E AGKISTRODON
L31          1277 S E1-E14
L32           243 S (AGKISTRO? OR A)()(CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MO
L33           227 S AGKISTRO? (L) (CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MOCCAS
L34         19855 S L28-L33
                  E VIPER/CT
                  E E4+ALL
L35             2 S E3,E4
                  E E28+ALL
L36           262 S E7+NT
L37           369 S E7-E12/BI
                  E E6+ALL
L38           615 S E6+NT
L39          1124 S E6-E35/BI
                  E VIPER
L40          2387 S E3,E4,E7,E8,E9,E10,E11
L41           447 S E13-E17,E22,E23,E24
                  E NOTECHIS/CW
L42           104 S E3
                  E NOTECHIS/CT
                  E E3+ALL
L43           104 S E6+NT
L44           162 S E6-E17/BI
                  E PSEUDONAJA/CT
                  E E3+ALL
L45            38 S E6+NT
L46            54 S E6-E12/BI
                  E OXYURANUS/CT
                  E E5+ALL
L47            77 S E6+NT
L48           122 S E6-E10/BI
L49         20335 S L34-L48
L50           976 S RUSSEL?(L)(SNAKE OR VIPER?)
L51           156 S COPPERHEAD OR COPPER HEAD
L52         20373 S L49-L51
L53            11 S L18 AND L52
                  E BLOOD COAGULATION/CT
                  E E3+ALL
L54         12573 S E7+NT
                  E BLOOD CLOT/CT
                  E E6+ALL
L55           483 S L52 AND L54
L56          2295 S L52 AND (?COAGUL? OR CLOT?)
L57          2295 S L55,L56
L58           168 S L52 AND (L1 OR PROTEIN C OR FACTOR XIV)
L59           158 S L52 AND (L2 OR PROTEIN C (L) ACTIV? OR FACTOR XIVA)
L60           157 S L58 AND L59
L61            42 S L60 AND (L3 OR FACTOR XA OR FACTOR X(L)ACTIV?)
L62             0 S L60 AND L8
L63             1 S L8
L64             1 S L60 AND (L4 OR ANTITHROMBIN III) AND (L5 OR HEPARIN (L) COFAC
L65           103 S L60 AND (L9 OR FACTOR X OR L10 OR PROTHROMBIN OR FACTOR II OR
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L66          24 S L60 AND (L21 OR CALCIUM(L)ION OR CA2# OR CA(L)ION)
L67          19 S L60 AND (L13 OR L14 OR L15 OR HEPARIN OR DERMATAN OR DEXTRAN(
L68          18 S L60 AND (L23 OR FACTOR(L)V (L) LEIDEN)
L69          76 S L61,L66-L68
L70          62 S L69 AND L65
L71          22 S L70 AND 9/SC
L72          16 S L69 AND BLOOD ANALYSIS/CT
L73           8 S L71 AND L72
L74           8 S L73 AND L24-L73
                SEL DN 3 5 6
L75           5 S L74 NOT E1-E3
L76         128 S L60 AND (PD<=19980202 OR PRD<=19980202 OR AD<=19980202)
L77          29 S L76 AND (BIOCHEM?(L)METHOD?)/SC,SX
L78          26 S L77 AND L61-L75
L79          68 S L76 AND L61-L75 NOT L77
L80          17 S L79 AND (SCREENING OR KIT OR FUNCTIONAL ASSAY OR COMPARISON O
L81           2 S L79 AND PROTAC/TI
L82           6 S L79 AND BLOOD ANALYSIS/CT
                SEL DN 5 6
L83           4 S L82 NOT E4-E5
L84          13 S L80 NOT L81-L83
                SEL DN 3 7 12 13
L85           9 S L84 NOT E6-E9
L86          31 S L20,L53,L63,L64,L75,L81,L83,L85
L87          59 S L69 AND L76
L88          46 S L87 NOT L86
                SEL DN 4 6 9 15 23 27 28 38 39
L89           9 S L88 AND E10-E18
L90          18 S L85,L89
L91          29 S L53,L90
L92          29 S L91 AND (?COAGUL? OR CLOT? OR FACTOR OR BLOOD OR PLASMA OR SE
L93          11 S L91 AND (RUSSEL? OR VIPER? OR PSEUDON? OR TEXTIL? OR NOTECH?
L94          29 S L92,L93 AND L16-L20,L24-L93
                SEL DN 20
L95          28 S L94 NOT E19

     FILE 'HCAPLUS' ENTERED AT 09:33:59 ON 13 MAY 2002
                SET COST ON
                SET COST OFF

     FILE 'BIOSIS' ENTERED AT 09:35:51 ON 13 MAY 2002
                E EXNER T/AU
L96         111 S E3,E4,E7,E8
L97       21433 S L26 OR L27 OR L30 OR L31 OR L32 OR L33  OR L37 OR L39 OR L40
L98          15 S L96 AND L97
L99          13 S 150?/CC AND L98
L100         13 S L98 AND PY<=1998
L101         11 S L99 AND L100
L102        101 S L96 NOT ARTICLE/DT
L103          2 S L102 AND PATENT/DT
L104         99 S L102 NOT L103
L105         10 S L101 AND L104
L106         12 S L103,L105
L107          5 S L98 NOT L106
                SEL DN L106 1-6
L108          6 S L106 AND E1-E6
L109          6 S L103,L108

     FILE 'BIOSIS' ENTERED AT 09:48:20 ON 13 MAY 2002
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